

University of Dundee

## Herpes simplex encephalitis

Bonnici-Mallia, Michael; Kanodia, Avinash Kumar; Rae, Nikolas; Marwick, Charis

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TITLE OF CASE
<h2>Herpes Simplex Encephalitis: Unusual Imaging Appearances</h2>
DESCRIPTION <i>Up to 250 words summarising the importance of the image(s)</i>
<p>Herpes Simplex Virus (HSV) is the most common non-epidemic and sporadic cause of viral meningoencephalitis with an incidence of approximately 1-3 cases per million. [1] 95% of fatal adult cases are a result of type 1 HSV (HSV-1) and typically follow latent viral reactivation in the trigeminal ganglion in immunocompetent patients. [1] Magnetic Resonance Imaging (MRI) is regarded as being the most sensitive radiological investigation, with changes usually visible within 2 to 3 days of onset of symptoms.[1] Traditionally on MRI, Herpes Simplex Encephalitis (HSE) exhibits bilateral asymmetrical involvement of the limbic system, including the medial temporal lobes, insular cortices, and infero-lateral frontal lobes and cingulate gyri.[1] Sparing of the basal ganglia is a key feature, which also helps in differentiating from middle cerebral artery infarction on DWI. Atypical patterns, if seen, usually affect the younger population with involvement of the cerebral hemispheres, and rarely, the midbrain and pons.[1]</p> <p>We present serial brain imaging of a 52 year old lady who presented to the acute medical unit with a week's history of lethargy, intermittent headaches and an episode of syncope prior to admission. Over the course of the subsequent 24 hours, she developed acute confusion and became hypotensive, hypothermic and bradycardic. Computed Tomography of the brain was not of any diagnostic value. MRI however demonstrated grossly abnormal signal change in the hypothalamic region at the floor of the third ventricle and optic chiasm and optic tracts on both sides, with partial involvement of the inferior aspect of the left putamen (Figure 1a-d). DWI showed a lesser degree of symmetrical restricted diffusion involving the para-median structures (Figure 1e,f). There was no significant enhancement with intravenous (IV) contrast (Figure 1g,h). The imaging findings were considered unusual and atypical for usually seen acute neurological conditions, although the possibility of Wernicke Encephalopathy was raised.</p> <p>Lumbar puncture for Cerebrospinal Fluid (CSF) examination revealed <math>94 \times 10^6/l</math> white cells (100% lymphocytes) with elevated CSF protein (<math>3042 \text{ mg/l}</math>) and normal CSF glucose (<math>4.2 \text{ mmol/l}</math>). Viral Polymerase Chain Reaction (PCR) on CSF was positive for HSV-1. The MRI scan was reviewed and upon literature review, no similar example of HSE was found with similar MRI findings; a possibility of false positive PCR was also raised, however, however sensitivity and specificity of PCR testing for HSV is accepted to exceed 95%.[2] Surprisingly, several clinical manifestations of HSE, such as cold sores, were also not present. However, there was no history of alcoholism or GI surgery to have predisposed the patient to Wernicke's encephalopathy.</p> <p>Patient was treated with antiviral therapy, although due to unusual MRI findings, intravenous thiamine was also given. Patient's hypothermia improved over the next few days and the patient subsequently developed fever. Clinical improvement followed over the course of 2 weeks. Two follow-up MRIs were performed over the next 8 weeks (Figure 2 and 3), that revealed an overall improvement in signal appearances in the hypothalamus, the left lentiform nucleus and optic chiasm and optic tracts, but residual changes in the form of subtle high signal persisted. Notably, the usual MRI features of HSE never developed. Four weeks after discontinuing antiviral medication, the patient developed unilateral acute retinal necrosis (ARN). The strong association</p>

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of ARN with herpesviruses [3] prompted further treatment with antiviral and immunosuppressive therapies. HSV-1 infection was subsequently again proven through positive vitreous PCR. Despite treatment, the present case resulted in cognitive impairment and the patient was subsequently transferred to a neuro-rehabilitation unit.

MRI is the modality of choice in imaging assessment of the hypothalamus.[4] Lesions affecting this region can be broadly classified into the following: neoplastic (primary and secondary), developmental, inflammatory/granulomatous diseases and lesions arising from the adjacent brain parenchyma.[4] Wernicke Encephalopathy is an acute neurological condition resulting from a dietary Vitamin B1 (thiamine) deficiency, and characteristically symmetrically involves the mamillary bodies, dorsomedial thalamus, tectal plate, periaqueductal area and the grey matter around the third and fourth ventricle.[5,6] It usually happens in a background of alcoholism or GI resection.

We have presented an unusual case of proven HSE, where the typical MRI findings were absent. There was hypothalamic involvement with hypothermia, which, to the best of our knowledge, has not been described before along with putamen involvement which is also rare. HSE should be included as a differential diagnosis when evaluating acute hypothalamic lesions on MRI.

## **LEARNING POINTS/TAKE HOME MESSAGE 2 to 3 bullet points – this is a required field**

- **HSE can rarely involve hypothalamus and present as hypothermia. It should be included in the differential of hypothalamic lesions.**
- **HSE may also involve putamen, although it is rare**
- **HSE can occur with absence of typical findings in temporal lobes and insula**

## **REFERENCES Vancouver style (max 3)**

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## **FIGURE/VIDEO CAPTIONS figures should NOT be embedded in this document**

Figure 1: Initial MRI findings. T2 axial (a), FLAIR coronal (b-d) show hypothalamic and floor of third ventricle involvement (white arrows), putamen involvement (black arrows), optic chiasm involvement (white broken arrow). DWI and ADC (c and d) show smaller areas of restricted

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diffusion (white arrows). T1 sagittal precontrast (g) and post contrast (h) show no enhancement.

Figure 2: Follow up MRI at 4 weeks. FLAIR coronal (a,b) and T2 axial (c) show improvement in hypothalamic signal (white arrow) and putemen (black arrow). DWI (d) shows reduced signal abnormality (white arrow).

Figure 3. Follow up MRI at 8 weeks. FLAIR coronal (a,b) and T2 axial (c) show further evolution of hypothalamic signal with subtle cavitation (white arrow) and putemen (black arrow). DWI (d) shows resolution of signal abnormality (white arrow).